# CENTER FOR DRUG EVALUATION AND RESEARCH

**Approval Package for:**

**Application Number : 074634**

**Trade Name : DOBUTAMINE HCL INJECTION**

**Generic Name: Dobutamine Hcl Injection 1250mg/100ml**

**Sponsor : Abbott Laboratories**

**Approval Date: September 27, 1996**

CENTER FOR DRUG EVALUATION AND RESEARCH

# APPLICATION 074634

## CONTENTS

| | Included | Pending Completion | Not Prepared | Not Required |
|---|---|---|---|---|
| **Approval Letter** | X | | | |
| **Tenative Approval Letter** | | | | |
| **Approvable Letter** | | | | |
| **Final Printed Labeling** | X | | | |
| **Medical Review(s)** | | | | |
| **Chemistry Review(s)** | X | | | |
| **EA/FONSI** | | | | |
| **Pharmacology Review(s)** | | | | |
| **Statistical Review(s)** | | | | |
| **Microbiology Review(s)** | | | | |
| **Clinical Pharmacology Biopharmaceutics Review(s)** | | | | |
| **Bioequivalence Review(s)** | X | | | |
| **Administrative Document(s)** | | | | |
| **Correspondence** | | | | |

# CENTER FOR DRUG EVALUATION AND RESEARCH

## Application Number 074634

## APPROVAL LETTER

ANDA 74-634

SEP 30 1996

9/27/96

Abbott Laboratories
Attention: Thomas F. Willer, Ph.D.
One Abbott Park Road, D-389, AP 30
Abbott Park, IL 60064-3537

Dear Sir:

This is in reference to your abbreviated new drug application dated February 28, 1995, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Dobutamine Hydrochloride Injection, 1250 mg (base)/100 mL vial (12.5 mg (base)/mL); Pharmacy Bulk Package.

Reference is also made to your amendments dated June 21, and July 30, 1996.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined that your Dobutamine Hydrochloride Injection, 1250 mg (base)/100 mL can be expected to have the same therapeutic effect as that of the reference listed drug product upon which the Agency relied as the basis of safety and effectiveness.

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final

printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-240). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-240) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

/S/ 9/27/96

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION NUMBER 074634

## FINAL PRINTED LABELING

100 mL NDC 0074-4729-01
(1250 mg Total)

# DOBUTAMINE
Hydrochloride Injection

Equivalent to Dobutamine
**12.5 mg/mL**

**CONTAINS NO PRESERVATIVE**

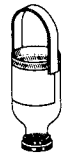
Pharmacy Bulk Package.
Not for Direct Infusion.

For I.V. use.*

*ABBOTT LABS., NORTH CHICAGO, IL 60064, USA*
RAO5278-2/R2-12/95

Each mL contains: dobutamine, hydrochloride equivalent to 12.5 mg dobutamine and sodium metabisulfite, 0.2 mg as antioxidant. May contain hydrochloric acid and/or sodium hydroxide for pH adjustment. pH 3.3 (2.5 to 5.5). Sterile, nonpyrogenic. Store at controlled room temperature 15° to 30°C (59° to 86°F).

Caution: Federal (USA) law prohibits dispensing without prescription.



Peel off the paper liner from both ends of the tape hanger to expose 3/4 inch long adhesive portions. Adhere each end to the label on the bottle. The vials should be suspended as a unit in the laminar flow hood.

*This pharmacy bulk package is intended for preparing I.V. admixtures only. See insert for complete dosage information and proper use of this container. **Discard vial 4 hours after initial entry.** A single entry through the vial closure should be made with a sterile dispensing set or transfer device. Transfer individual doses to appropriate intravenous infusion solutions. Use of a syringe with needle is not recommended. The above process should be carried out under a laminar flow hood using aseptic technique.



Printed in USA

++300744729012Z

100 mL NDC 0074-4729-01
(1250 mg Total)

DOBUTAMINE
Hydrochloride Injection

Equivalent to Dobutamine
12.5 mg/mL

Pharmacy Bulk Package.
Not for Direct Infusion.

For I.V. use.*

100 mL (1250 mg Total)

# DOBUTAMINE

Hydrochloride Injection

Equivalent to Dobutamine

**12.5 mg/mL**

**CONTAINS NO PRESERVATIVE**

Pharmacy Bulk Package.
Not for Direct Infusion.

For I.V. use.*

*ABBOTT LABORATORIES, NORTH CHICAGO, IL 60064, USA*

NDC 0074-4729-01

Date Entered _____ Time _____

Each mL contains: dobutamine hydrochloride equivalent to 12.5 mg dobutamine and sodium metabisulfite 0.2 mg as antioxidant. May contain hydrochloric acid and/or sodium hydroxide for pH adjustment. pH 3.3 (2.5 to 5.5). Sterile, nonpyrogenic. *This pharmacy bulk package is intended for preparing I.V. admixtures only. See insert for complete dosage information and proper use of this container. **Discard vial 4 hours after initial entry.** A single entry through the vial closure should be made with a sterile dispensing set or transfer device. Transfer individual doses to appropriate intravenous infusion solutions. Use of a syringe with needle is not recommended. The above process should be carried out under a laminar flow hood using aseptic technique. Store at controlled room temperature 15° to 30°C (59° to 86°F). Caution: Federal (USA) law prohibits dispensing without prescription.

 RAO5276-2/R2 12/95 Printed in USA

DOBUTAMINE HCl Inj.
1250 mg Total (12.5 mg/mL)

++30074729011Y

# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION NUMBER 074634

## CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 3 2. ANDA #74-634

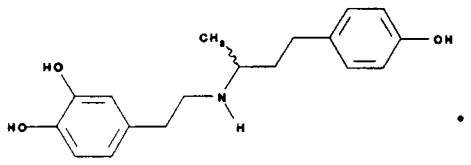
3. NAME AND ADDRESS OF APPLICANT
Abbott Laboratories
Attention: Thomas F. Willer, Ph.D.
One Abbott Park Road
Abbott Park, IL 60064-3547

4. BASIS OF SUBMISSION Dobutrex® solution; Eli Lilly and the ANDA Suitability Petition by Marsam Pharmaceuticals, Inc.

5. SUPPLEMENT(s) N/A
6. PROPRIETARY NAME none
7. NONPROPRIETARY NAME **Dobutamine Hydrochloride Injection**

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A
9. AMENDMENTS AND OTHER DATES:
February 28, 1995 Date of application.
June 21, 1996: Amendment
July 30, 1996: Telephone Amendment
10. PHARMACOLOGICAL CATEGORY Cardiotonic
11. Rx or OTC Rx
12. RELATED IND/NDA/DMF(s) See sec. 37 for DMFs
**ANDA 74-086**; Abbott Dobutamine HCl Injection; 12.5 mg/mL; 20 mL fill

13. DOSAGE FORM inj. 14. POTENCY **12.5 mg/mL; 100 mL vial**
15. CHEMICAL NAME AND STRUCTURE
Dobutamine Hydrochloride USP
$C_{18}H_{23}NO_3.HCl$; M.W. = 337.85
(±)-4-[2-[[3-(*p*-Hydroxyphenyl)-1-methylpropyl]amino]ethyl]pyrocatechol hydrochloride. CAS [49745-95-1]




16. RECORDS AND REPORTS N/A

18. CONCLUSIONS ANDRE COMMENDATIONS: App rovable

See Comments Section.

19. REVIEWER: Devinder S. Gill DATE COMPLETED: July 2, 1996

cc: ANDA 74-634
ANDA 74-634/DUP/Division File
Field Copy
Endorsements:
HFD-623/D.Gill/7-2-96
HFD-623/V.Sayeed, Ph.D.
X:\new\firmsam\abbott\[illegible]
F/T by: bc/9-16-96

/S/ 9/16/96

D.N

ANDA 74-634

AUG 31 1995

Abbott Laboratories
Attention: Frederick A. Gustafson
One Abbott Park Road
Abbott Park, IL 60064-3547

Dear Sir:

Reference is made to the request for waiver of *in vivo* bioequivalence, submitted for Dobutamine Hydrochloride for Injection USP, 12.5 mg (eq. base)/mL (100 mL vial, pharmacy bulk package).

The Office of Generic Drugs has reviewed the waiver request and has found it to be incomplete for the following reason:

There are data discrepancies found in the submission. Though the application is for Dobutamine Hydrochloride, on page 1-12 of volume 1.1 and pages 1-28 of volume 1.1, reference is made to the formulation of Stadol® (Butorphanol Tartrate Injection, USP), 1 mg/mL. The Office notes that this could be a type error. Abbott, should review the application and ensure that this discrepancy is not repeated through-out the application, and ensure the data contained in the application is specific for Dobutamine.

As described under 21 CFR 314.96 an action which will amend this application is required, if you have any questions, please call Jason A. Gross, Pharm.D., at (301) 594-2290. In future correspondence regarding this issue, please include a copy of this letter.

Sincerely yours,

Keith K. Chan, Ph.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation
and Research

# CENTER FOR DRUG EVALUATION AND RESEARCH

## APPLICATION NUMBER 074634

## BIOEQUIVALENCE REVIEW(S)

AUG 15 1995

Dobutamine Hydrochloride Injection
12.5 mg/mL 100 mL Vial (PBP)
ANDA #74-634
Reviewer: Moheb H. Makary
WP. 74634W.295

Abbott Laboratories
Abbott Park, Illinois
Submission Date:
February 28, 1995

## Review of a Waiver Request

I. Objective:

The firm has requested a waiver of bioequivalence study requirements for its product Dobutamine Hydrochloride Injection, 12.5 mg/mL, 100 mL Vial, Pharmacy Bulk Package (PBP). Innovator product is Dobutrex® 12.5 mg/mL, 20 mL Vial, manufactured by Eli Lilly. Dobutamine Hydrochloride Injection, 12.5 mg/mL, 100 mL Vial, Pharmacy Bulk Package (PBP), as a new strength, was the subject of an ANDA Suitability Petition by Marsam Pharmaceuticals, Inc., Dock Number 93 P-0045/CP1. The Agency approved this petition on September 10, 1993. The firm included a copy of the FDA approval letter in the submission.

II. Deficiency Comments:

The firm stated on page 1-28 of the submission " A comparison of currently approved Stadol® (Butorphanol Tartrate Injection, USP), 1 mg/mL, product by Bristol Laboratories and the proposed formula Butorphanol Tartrate Injection, USP, 1 mg/mL". Below this statement a quantative formulation comparison between Abbott's Dobutamine Hydrochloride Injection and the brand product, Dobutrex® (Lilly) was listed.
The firm is advised to clarify the discrepancies on pages 1-12 and 1-28.

III. Recommendation:

The waiver of in vivo bioequivalence study requirements for the test product is pending the firm's clarification.

The firm should be informed of the deficiency comment and recommendation

/S/

Moheb H. Makary, Ph.D.
Division of Bioequivalence
Review Branch III

RD INITIALLED RMHATRE
FT INITIALLED RMHATRE

/S/

Date: 8/3/95

Concur: /S/ Date: 8/15/95

Keith
Director
Division of Bioequivalence

MMakary/8-2-95 wp 74634W.295
cc: ANDA #74-634, original, HFD-600 (Hare), HFD-630, HFC-130 (JAllen), HFD-344 (CViswanathan), HFD-658 (Mhatre, Makary), Drug File, Division File.